REMARKS

Following the amendment, claims 1-5, 7-10, and 12-34 are pending. Claim 26 is currently amended. Claims 31-34 are newly added. Claims 6 and 11 were previously canceled. Claim 26 has been amended to recite that the NT embryo is transferred "to a host mammal of the same species" and claim 27 has been amended to recite that culturing the NT embryo is "prior to transfer of the NT embryo to a host mammal of the same species," which amendments find support at least in original claim 28 and on page 20, lines 15-16. New claims 31-34 find support at least in claim 1 and in original claims 15, 20, 21, and 22, respectively.

Applicant appreciates the Examiner's observation in her December 17, 2007 Office Action that claims 15 and 20-22 are free of the prior art and would be allowable if written in independent form. Applicant has added new independent claims 31-33 that incorporate the limitations of the claims 15, 20, and 21 and of base claim 1, as well as new dependent claim 34 based on original claim 22, and trusts that the claims are now in condition for allowance.

Rejections Under 35 U.S.C. 112, First Paragraph (Enablement)

The Office Action rejects claims 26-30 on the ground that the specification allegedly does not enable production of a cloned mammal unless the NT unit is transferred to the uterus of a host female mammal of the same species. Applicant first notes that claims 28-30 are limited to production of a cloned mammal by transferring the NT unit to the uterus of a host female mammal of the same species (see text of claim 28). Therefore, Applicant submits that the present ground of rejection does not apply to claims 28-30.

Notwithstanding this, Applicant notes that claim 26 has been amended to recite that the NT embryo is transferred "to a host mammal of the same species" and that claim 27 has been amended to recite that culturing the NT embryo is "prior to transfer of the NT embryo to a host mammal of the same species." Applicant submits that claims 26 and 27 (and claims 28-30 which depend from claim 27) are now limited to subject matter indicated in the Office Action as being enabled and trusts that it has overcome the rejection.

Rejections Under 35 U.S.C. § 103

Claims 1-5, 7, 9, 10, 14, 16, 17, 19 and 23-30 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cibelli et al. (1998) Science, Vol. 280, pp. 1256-1258, or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418, in view of Kwon et al. (1996) Prod. Natl. Acad. Sci., Vol. 93, pp. 13010-13013.

Claims 1 and 7-9 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cibelli et al. (1998) Science, Vol. 280, pp. 1256-1258, or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418, in view of Kwon et al. (1996) Prod. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 and further in view of Wakayama et al. (1998) Nature, Vol. 394, pp. 369-374.

Claims 1, 12, and 13 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cibelli et al. (1998) Science, Vol. 280, pp. 1256-1258, or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418, in view of Kwon et al. (1996) Prod. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 and further in view of Campbell et al. (1994) Biology of Reproduction, Vol. 50, pp. 1385-1393.

Claims 1 and 18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cibelli et al. (1998) Science, Vol. 280, pp. 1256-1258, or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418, in view of Kwon et al. (1996) Prod. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 and further in view of Yang et al. (1992) Biology of Reproduction, Vol. 42, Supp. 1, p. 117, Abstract 268.

The U.S. Patent and Trademark Office has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *See In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177 (C.C.P.A. 1967); *In re Fine,* 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988). In rejecting a claim under 35 U.S.C. § 103, the Examiner must establish a *prima facie* case that: (i) the prior art suggests the claimed invention; and (ii) the prior art indicates that the invention would have a reasonable likelihood of success. *See In re Dow Chemical Company,* 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988).

Cibelli or Prater in view of Kwon

All of the rejections under 35 U.S.C. § 103(a) rely on the same combination of Cibelli or Prather, each in view of Kwon. However, neither the combination of Cibelli and Kwon nor the combination of Prather and Kwon supports a prima facie case of obviousness against the claims. In particular, nothing in the references discloses or suggests the use of differentiated metaphase cells for the donor genetic material. Further, nothing in the references discloses or suggests that metaphase donor genetic material from a differentiated cell could be successfully used as the source of genetic material in a nuclear transfer operation.

Cibelli in view of Kwon

Cibelli discloses a method of nuclear transfer using fibroblast cells as the donor genetic material but does not disclose or suggest use of metaphase cells. Kwon discloses a method of nuclear transfer using only undifferentiated donor material (4-cell embryos). The Office Action states that Cibelli provides motivation in stating that the properties of the donor cell are important even though the cell cycle state of the donor in the nuclear transfer experiments is unknown. Applicant submits that this does not provide any suggestion or motivation to use metaphase cells (or any other particular cell cycle phase). Further, Cibelli states that "more work will be necessary to understand the properties of somatic cells required to allow for successful reprogramming and full term development of offspring" (page 1257, column 3, third paragraph). This is inconsistent with the conclusion drawn in the Office Action. Cibelli does not disclose or suggest the use of donor genetic material of any particular cell cycle phase.

The Office Action states that Kwon provides motivation in teaching that 27% of the transferred mouse reconstructed embryos developed to term. Applicant submits that this only provides motivation to use the specific method of Kwon (using undifferentiated donor genetic material) and does not suggest which feature of the Kwon method might be the source of the high success rate (in fact, a far as can be determined from Kwon, all of the features of the method in combination could be responsible for the high success rate). Further, success with undifferentiated donor genetic material, which does not require the reprogramming required

for differentiated genetic material, says little relevant to guide those wishing to use undifferentiated donor genetic material. Thus, Kwon does not provide any suggestion or motivation to use either differentiated donor genetic material in general or differentiated donor genetic material of any particular cell cycle phase.

The combination of Cibelli and Kwon does not bridge the gap left by each. In particular, neither Cibelli nor Kwon, either alone or in combination, disclose or suggest using differentiated donor genetic material of any particular cell cycle phase in a nuclear transfer method. Although the Office Action states that the ordinary artisan would have sought enhanced success rates of nuclear transfer by combining the cited art, the cited art fails to indicate what features might improve the success rate and fails to provide any likelihood of success in such a combination. Further, those of ordinary skill in the art would likely attribute the difference in success rates between Kwon and Cibelli to the difference between undifferentiated (Kwon) and fibroblast (Cibelli) donor genetic material rather than the cell cycle stage. Applicant also notes that, although Cibelli was published two years after Kwon, Cibelli draws no conclusions from Kwon's use of metaphase donor genetic material. Rather, Cibelli leaves the cell cycle stage of donor genetic material indeterminate. This is inconsistent with Kwon providing any suggestion or motivation for the use of metaphase donor genetic material when differentiated donor genetic material is used.

Because Cibelli and Kwon fail to disclose, suggest or provide motivation to use all of the claimed features, and because Cibelli and Kwon fail to provide a likelihood of success, Cibelli and Kwon fail to supports a prima facie case of obviousness against the claims and in particular against claims 1-5, 7, 9, 10, 14, 16, 17, 19 and 23-30.

Prather in view of Kwon

Prather discloses a method of nuclear transfer using undifferentiated cells as the donor genetic material (pig 2-, 4-, or 8-cell embryos). Kwon discloses a method of nuclear transfer using only undifferentiated donor material. Thus, neither Prather nor Kwon disclose or suggest the use of differentiated donor genetic material. The Office Action states that Prather provides motivation in stating that the cell cycle stage of the embryo that is the donor nucleus

may be important in successful cloning. Applicant submits that this does not provide any suggestion or motivation to use differentiated donor genetic material. Further, Prather states that a "major developmental difference between these animal embryos is the timing of the transition from maternal control of development (relying upon maternally stored RNA) to zygotic control of development (relying on zygotically produced RNA)" (page 416). This teaches away from the use of differentiated donor genetic material and is inconsistent with the conclusion drawn in the Office Action. Prather does not disclose or suggest the use of differentiated donor genetic material.

The Office Action states that Kwon provides motivation in teaching that 27% of the transferred mouse reconstructed embryos developed to term. Applicant submits that this only provides motivation to use the specific method of Kwon (using undifferentiated donor genetic material) and does not suggest which feature of the Kwon method might be the source of the high success rate (in fact, a far as can be determined from Kwon, all of the features of the method in combination could be responsible for the high success rate). Further, success with undifferentiated donor genetic material, which does not require the reprogramming required for differentiated genetic material, says little relevant to guide those wishing to use undifferentiated donor genetic material and does not provide a reasonable expectation of success if differentiated donor genetic material was used. Thus, Kwon does not provide any suggestion or motivation to use either differentiated donor genetic material in general or differentiated donor genetic material of any particular cell cycle phase.

The combination of Prather and Kwon does not bridge the gap left by each. In particular, neither Prather nor Kwon, either alone or in combination, disclose or suggest using differentiated donor genetic material in a nuclear transfer method. Although the Office Action states that the ordinary artisan would have sought enhanced success rates of nuclear transfer by combining the cited art, the cited art fails to indicate what features might improve the success rate and fails to provide any likelihood of success in such a combination. Because Prather and Kwon fail to disclose, suggest or provide motivation to use all of the claimed features, and because Prather and Kwon fail to provide a likelihood of success, Prather and Kwon fail to

supports a prima facie case of obviousness against the claims and in particular against claims 1-5, 7, 9, 10, 14, 16, 17, 19 and 23-30.

Cibelli or Prater in view of Kwon and Wakayama

The rejection under 35 U.S.C. § 103(a) of claims 1 and 7-9 relies on the same combination of Cibelli or Prather, each in view of Kwon, as discussed above. As discussed above, neither the combination of Cibelli and Kwon nor the combination of Prather and Kwon supports a prima facie case of obviousness against the claims. In particular, nothing in the references discloses or suggests the use of differentiated metaphase cells for the donor genetic material. Further, nothing in the references discloses or suggests that metaphase donor genetic material from a differentiated cell could be successfully used as the source of genetic material in a nuclear transfer operation.

Wakayama discloses, and was relied on in the rejection for it disclosure of, the use of cumulus cells as the donor genetic material. Wakayama fails to disclose or suggest the use of metaphase donor genetic material. Thus, Wakayama fails to fill the gaps left by the combination of Cibelli and Kwon or the combination of Prather and Kwon. Nothing in any of the references discloses or suggests the use of differentiated metaphase cells for the donor genetic material. Further, nothing in the references discloses or suggests that metaphase donor genetic material from a differentiated cell could be successfully used as the source of genetic material in a nuclear transfer operation.

Kwon expresses a clear preference for undifferentiated donor genetic material and Wakayama states a clear preference for G0 or G1 donor genetic material. As stated by Wakayama, "[p]revious studies have suggested that embryonic development is enhanced when donor nuclei are in the G0 or G1 phase of the cell cycle. [Based on these studies, we] have investigated the development potential of oocytes injected with the nuclei of non-cultured cells known to be at G0." As with Cibelli, although Wakayama was published two years after Kwon, Wakayama draws no conclusions from Kwon's use of metaphase donor genetic material. Rather, Wakayama states a clear preference for G0 or G1 donor genetic material, which amounts to a teaching away from the use of cells in other cell cycle stages. This is

inconsistent with Wakayama providing any suggestion or motivation for the use of metaphase donor genetic material when differentiated donor genetic material is used. Also as with Cibelli, those of ordinary skill in the art would likely attribute the difference in success rates between Kwon and Wakayama to the difference between undifferentiated (Kwon) and somatic (Wakayama) donor genetic material rather than the cell cycle stage.

Because Cibelli, Kwon, and Wakayama fail to disclose, suggest or provide motivation to use all of the claimed features, and because Cibelli, Kwon, and Wakayama fail to provide a likelihood of success, Cibelli, Kwon, and Wakayama fail to supports a prima facie case of obviousness against claims 1 and 7-9. Similarly, because Prather, Kwon, and Wakayama fail to disclose, suggest or provide motivation to use all of the claimed features, and because Prather, Kwon, and Wakayama fail to provide a likelihood of success, Prather, Kwon, and Wakayama fail to supports a prima facie case of obviousness against claims 1 and 7-9.

Cibelli or Prater in view of Kwon and Campbell

The rejection under 35 U.S.C. § 103(a) of claims 1, 12, and 13 relies on the same combination of Cibelli or Prather, each in view of Kwon, as discussed above. As discussed above, neither the combination of Cibelli and Kwon nor the combination of Prather and Kwon supports a prima facie case of obviousness against the claims. In particular, nothing in the references discloses or suggests the use of differentiated metaphase cells for the donor genetic material. Further, nothing in the references discloses or suggests that metaphase donor genetic material from a differentiated cell could be successfully used as the source of genetic material in a nuclear transfer operation.

Campbell discloses, and was relied on in the rejection for it disclosure of, activation of the recipient oocyte prior to and at the same time as introduction of the donor genetic material. Campbell discloses use of undifferentiated unsynchronized donor genetic material. Campbell fails to disclose or suggest the use of differentiated metaphase donor genetic material. Thus, Campbell fails to fill the gaps left by the combination of Cibelli and Kwon or the combination of Prather and Kwon. Nothing in any of the references discloses or suggests the use of differentiated metaphase cells for the donor genetic material. Further, nothing in the

references discloses or suggests that metaphase donor genetic material from a differentiated cell could be successfully used as the source of genetic material in a nuclear transfer operation.

Because Cibelli, Kwon, and Campbell fail to disclose, suggest or provide motivation to use all of the claimed features, and because Cibelli, Kwon, and Campbell fail to provide a likelihood of success, Cibelli, Kwon, and Campbell fail to supports a prima facie case of obviousness against claims 1, 12, and 13. Similarly, because Prather, Kwon, and Campbell fail to disclose, suggest or provide motivation to use all of the claimed features, and because Prather, Kwon, and Campbell fail to provide a likelihood of success, Prather, Kwon, and Campbell fail to supports a prima facie case of obviousness against claims 1, 12, and 13.

Cibelli or Prater in view of Kwon and Yang

The rejection under 35 U.S.C. § 103(a) of claims 1 and 18 relies on the same combination of Cibelli or Prather, each in view of Kwon, as discussed above. As discussed above, neither the combination of Cibelli and Kwon nor the combination of Prather and Kwon supports a prima facie case of obviousness against the claims. In particular, nothing in the references discloses or suggests the use of differentiated metaphase cells for the donor genetic material. Further, nothing in the references discloses or suggests that metaphase donor genetic material from a differentiated cell could be successfully used as the source of genetic material in a nuclear transfer operation.

Yang discloses, and was relied on in the rejection for it disclosure of, activation of the recipient oocyte using cycloheximide. Yang fails to disclose or suggest the use of differentiated metaphase donor genetic material. Thus, Yang fails to fill the gaps left by the combination of Cibelli and Kwon or the combination of Prather and Kwon. Nothing in any of the references discloses or suggests the use of differentiated metaphase cells for the donor genetic material. Further, nothing in the references discloses or suggests that metaphase donor genetic material from a differentiated cell could be successfully used as the source of genetic material in a nuclear transfer operation.

Because Cibelli, Kwon, and Yang fail to disclose, suggest or provide motivation to use all of the claimed features, and because Cibelli, Kwon, and Yang fail to provide a likelihood of

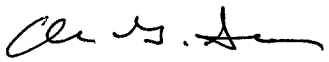
success, Cibelli, Kwon, and Yang fail to supports a prima facie case of obviousness against claims 1 and 18. Similarly, because Prather, Kwon, and Yang fail to disclose, suggest or provide motivation to use all of the claimed features, and because Prather, Kwon, and Yang fail to provide a likelihood of success, Prather, Kwon, and Yang fail to supports a prima facie case of obviousness against claims 1 and 18.

CONCLUSION

It is respectfully submitted that this application is in condition for allowance, and an early notification to that effect is respectfully requested. If any issues remain that can be resolved with an Examiner's Amendment or a telephone conference, please contact the undersigned at 404-873-8512.

A credit card charge in the amount of $890.00, representing $525.00 for the fee for a small entity under 37 C.F.R. § 1.17(a)(3), $50.00 for the fee for a small entity under 37 C.F.R. § 1.16(i), and $315.00 for the fee for a small entity under 37 C.F.R. § 1.16(h), and a Request for Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 012506.

Respectfully submitted,



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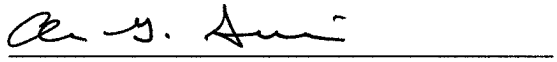

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